UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/717,573	11/21/2003	Jen-Leih Wu	33151-188802	3665

23639 7590 08/22/2007

BINGHAM MCCUTCHEN LLP
Three Embarcadero Center
San Francisco, CA 94111-4067

EXAMINER	
MITCHELL, LAURA MCGILLEM	
ART UNIT	**PAPER NUMBER**
1636	
MAIL DATE	**DELIVERY MODE**
08/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/717,573	WU ET AL.	
	Examiner	Art Unit	
	Laura M. Mitchell	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-7, 10-14 and 30-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *32-36* is/are allowed.

6)☒ Claim(s) *5-7,10-14,30 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/29/2007 has been entered.

It is noted that claims 5-7, 12 and 14 have been amended, claims 1-4, 8-9 and 15-29 are canceled and claims 30-36 have been added. Claims 5-7, 10-14 and 30-36 are under examination.

Priority

It is noted that this Application receives priority benefit of provisional Application No. 60/463,035, filed 4/16/2003. While Application No. 60/463,035 discloses a construct comprising a 2.8kb 5' flanking region of the L-FABP gene operably linked to a gene encoding EGFP, it does not specifically disclose the specific regions of sequences for the claimed binding sites (e.g. PDX1, PDX2, HFH(1), HFH(2), hnf-1α or HNF-3β). In addition, the Application does not specify any SEQ ID NOs.

It is noted that this Application also receives priority benefit of U.S. Provisional Patent Application No. 60/473,210, filed 5/27/2003. Application No. 60/473,210 does specifically disclose the specific regions of sequences for the claimed binding sites (e.g.

PDX1, PDX2, HFH(1), HFH(2), HNF-1α or HNF-3β). Claims that recite these regions will be given priority benefit of 5/27/2003.

Claim Objections

Claim 30 is objected to because of the following informalities: Claim 30 appears to be grammatically incorrect. Claim 30 recites the phrase: "HFH(1) binding site is in an upstream binding region of said HFH(2) binding site, said HFH(2) binding site is in an upstream region of said HNF-1α binding site, and said HNF- 1α binding site is in an upstream region of said HNF-3β binding site". As written, the claim could be interpreted that, for example, the HFH(1) binding site is part of the HFH(2) binding site. Since the specification does not disclose that the binding regions overlap with one another, it appears that the phrasing "site is **in** an upstream region **of** said ..... binding site" (for example) may be a grammatical error. For examination purposes, the claim will be interpreted as if the phrasing is "site is in a region upstream from said .... binding site". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-7, 10-14 and 30-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains

subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Previously rejected claims 1, 3-4 and 8-9 have been canceled.

This rejection is being maintained for reasons of record in the previous Office Action mailed 1/29/2007 and for reasons outlined below.

Applicants have added claim 30 to replace the original claim 1, and have further added the order of HFH(1), HFH(2), HNF-1α, and HNF-3β binding sites in the liver-specific expression control sequence to the claims. Applicants submit that this amendment is fully supported by the specification on pages 39-40, and Figures 11-13. Claim 31 is added to further limit the size of the liver-specific expression control sequence *(i.e.,* at least 435 bps) and the location of the liver-specific expression control sequence *(i.e.,* from an upstream region of a gene encoding a zebrafish L-FABP). Applicants submit that this amendment is fully support throughout the specification, in SEQ ID NO: 1, and by the original claim 7.

Applicant's arguments filed 8/15/2006 have been fully considered but they are not persuasive. New claim 30 is drawn to an isolated polynucelotide comprising a liver-specific expression control sequence from a zebrafish. Although claim 30 limits the order of the binding sites comprised in the claimed polynucleotide, claim 30 does not put any limitation of the size of the isolated polynucleotide that would be a liver-specific expression control sequence, and therefore the claimed isolated polynucleotide encompasses a very large genus of polynucleotides comprising a liver-specific

expression control sequence in which the binding sites can be at any distance from one another. Claim 31 is drawn to the polynucleotide, wherein the sequence contains at least 435 base pairs. In the instant disclosure, a 435 bp nucleotide sequence identified as SEQ ID NO:1 (or LR) comprises the binding regions for HFH(1), HFH(2), HNF-1α and HNF-3β. These regions were identified by sequence analysis. However, as claim 31 is written, it does not require that the sequences identifed as SEQ ID NO:4-7 be comprised within the 435 base pairs, rather it only provides a minimum length for the expression control sequence.

In order for the written description requirement to be satisfied it must include description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed invention. The function of the claimed polynucleotide expression control sequence is that it modulates expression of a vertebrate liver FABP. Modulation of expression is a broad term. The instant specification discloses that the 435 bp nucleotide sequence "does not, by itself, direct liver-specific transcription" (see paragraph 0094). Instead, it must be in association with a basal promoter. In the specification, longer sequences are identified as liver-specific expression control sequences (SEQ ID NOs 2-3) but Applicants disclose that the 435 nucleotide sequence functions in a liver-specific manner if associated with any core promoter included from the CNV or RSV viruses.

The claims drawn to a polynucleotide comprising sequences of binding regions for HFH(1), HFH(2), HNF-1 α and HNF-3β suggests that they are essential and sufficient for the function of modulating L-FABP expression. The instant specification does not sufficiently describe or establish a structure/functional relationship for the HFH(1), HFH(2), HNF-1α and HNF-3β binding regions and the claimed function of modulating the expression of a L-FABP. The instant specification discloses serial deletion experiments to analyze function of the expression control sequence. Example II discloses a serial deletion analysis of the upstream region of the L-FABP that demonstrates the importance of the 435 nucleotide sequence. Specifically Applciants demostrate that the deletion of either of the two HFH sites or the HNF-1α site or the HNF-3β element altered specificity in the liver primordia of fish larva (see paragraph 0164) The deletion studies show the motifs PDX1 (1) and PDX1(2) are not required for efficient liver-specific gene expression.

In the instant case, the specification discloses polynucleotides (SEQ ID NOs:1-3) comprising liver-specific expression control sequences that comprise the four binding sites in a particular orientation in the sequence for the claimed liver-expression control sequence from a zebrafish. There is no indication that any other sequences that would comprise SEQ ID NOs: 4-9 at any distance from each other would have the function of modulation of expression of a vertebrate L-FABP. There is no description of mutational sites which naturally occur in the molecule and there is no description of how the structure of the disclosed polynucleotide relates to the structure of any other polynucleotide that comprises HFH(1), HFH(2), HNF-1α and HNF-3β binding regions at

any distance from each other or separate from a basal promoter. The applicant does not provide an indication of how the sequences of SEQ ID NOs:1-3 comprising a 435 bp sequence comprising HFH(1), HFH(2), HNF-1α and HNF-3β binding regions is representative of other liver-expression control sequence that modulate expression. Other common attributes of the liver-expression control sequences are not described and the identifying attributes of the individual polynucleotide that are liver-expression control sequence are not described. Therefore, there is not a structural and functional basis provided by the prior art or the specification for one of ordinary skill in the art to envision all liver-expression control sequences that would comprise HFH(1), HFH(2), HNF-1α and HNF-3β binding regions upstream form one another in the order as written. According to these facts, one of skill in the art would conclude that applicant was not in possession of the claimed genus because a description of only one member of this genus is not representative of the variant of the genus and is insufficient to support them.

Claim Rejections - 35 USC § 102

Claims 1-4 and 8-9 have been canceled and claim 12 has been amended to depend from newly added claim 30. Newly added claim 30 is drawn to an isolated polynucleotide comprising binding sites having the nucleotide sequences of SEQ ID NOs: 4-7. Claim 5 has been amended to depend from claim 30 and is drawn to the polynucleotide wherein the sequence further comprises the nucleotide sequences of SEQ ID NO:8-9.

These specific sequences of SEQ ID NOs:4-9 are not taught in Zhong et al. Therefore the rejection of claims 5-7, 10-12 and 14 under 35 U.S.C. 102(b) as being anticipated by Zhong et al (Genomics, 1998, of record) is withdrawn.

The rejection of claims 12 and 14 under 35 U.S.C. 102(a) as being anticipated by Genbank Accession No. AL929535, submitted by Tracey is withdrawn. In a STIC search, the sequences identified as SEQ ID NOs: 4-9 were aligned with Genbank Accession No. AL929535. Only SEQ ID NO:5 has a 100% identity with a portion of AL929535. The other SEQ ID NOs display identities of 95.2% or less to AL929535. Thus, AL929535 does not anticipate an isolated polynucleotide sequence that comrpises the nucleotide sequences of SEQ ID NOs: 4-9.

The rejection of claims 12 and 14 under 35 U.S.C. 102(a) as being anticipated by Genbank Accession No. AC139623, submitted by Akhter et al is withdrawn. In a STIC search, the sequences identified as SEQ ID NOs: 4-9 were aligned with Genbank Accession No. AC139623 (Akhter et al). Only SEQ ID NOs:5 and 8 have a 100% identity with a portion of AC139623. The other SEQ ID NOs display identities of 95.2% or less to AC139623. Therefore, AC139623 does not anticipate an isolated polynucleotide sequence that comrpises the nucleotide sequences of SEQ ID NOs: 4-9.

The rejection of claim 1 (now cancelled) under 35 U.S.C. 102(a) as being anticipated by Genbank Accession No. BX240588, Humphray et al is mooted and

withdrawn. It is noted that in a STIC search, the sequences identified as SEQ ID NOs: 4-9 were aligned with Genbank Accession No. BX240588. Results showed that only SEQ ID NO:5 has a 100% identity with a portion of BX240588. The other SEQ ID NOs display identities of 95.2% or less to BX240588. Therefore, BX240588 does not anticipate an isolated polynucleotide sequence that comrpises the nucleotide sequences of SEQ ID NOs: 4-9.

Conclusion

Claims 32-36 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura M. Mitchell whose telephone number is (571) 272-8783. The examiner can normally be reached on M-F 8:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the

Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Laura McGillem Mitchell, PhD
Examiner
8/15/2007

CELINE QIAN, PH.D.
PRIMARY EXAMINER